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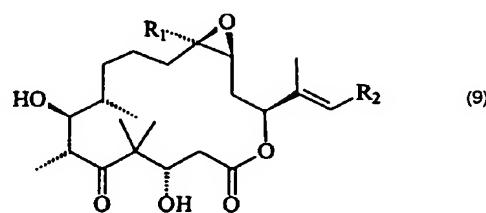
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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: A NEW PROCESS FOR THE PREPARATION OF EPOTHILONE DERIVATIVES, NEW EPOTHILONE DERIVATIVES AS WELL AS NEW INTERMEDIATE PRODUCTS FOR THE PROCESS AND THE METHODS OF PREPARING SAME



(57) Abstract: The present invention provides a synthesis for the preparation of epothilone derivatives of formula (9) wherein R1 is methyl, and R2 has the meaning of an unsubstituted or substituted aryl, an unsubstituted or substituted heteroaryl or an unsubstituted or substituted heterocyclic radical fused to a benzene nucleus, and salts thereof, and intermediates for the synthesis of a compound of formula (9).

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INTERNATIONAL SEARCH REPORT

National Application No

PCT/EP 10171

| | | | | | |
|-------------------------------------|------------|------------|------------|------------|-----------|
| A. CLASSIFICATION OF SUBJECT MATTER | | | | | |
| IPC 7 | C07D493/04 | C07D303/14 | C07D303/16 | C07D275/06 | A61P35/00 |

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

PAJ, EPO-Internal, WPI-Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|--|-----------------------|
| P, X | WO 2004/012735 A (BERGER MARKUS ;BOSSLER KLAUS (DE); KLAR ULRICH (DE); SCHERING AG () 12 February 2004 (2004-02-12) Caplus-RN: 658054-18-3 --- | 21, 22, 34 |
| X | WO 01/07439 A (MARTIN HARRY ;MULZER JOHANN (DE); SCHERING AG (US)) 1 February 2001 (2001-02-01) page 33, 34: compound 22 --- | 21, 22 |
| X | WO 99/54330 A (SQUIBB BRISTOL MYERS CO) 28 October 1999 (1999-10-28) page 23, compound below --- | 21, 22 -/- |

Further documents are listed in the continuation of box C.

Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubt on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the International filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

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ru/EP 3/10171

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

| Category | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|----------|---|-----------------------|
| X | HOEFLER G ET AL: "EPOTHILONE A-D AND THEIR THIAZOLE-MODIFIED ANALOGS AS NOVEL ANTICANCER AGENTS" PURE & APPLIED CHEMISTRY, PERGAMON PRESS, OXFORD, GB, vol. 71, no. 11, 1999, pages 2019-2024, XP001008755 ISSN: 0033-4545 page 2022, compound 15a --- | 21,22 |
| A | WO 98/25929 A (CIBA GEIGY AG ; SARABIA FRANCISCO (ES); VALLBERG HANS (SE); NICOLAO) 18 June 1998 (1998-06-18) cited in the application page 1, 1st paragraph, page 47, formula XIII, figure 56, compound 356a claims 1-15 --- | 1-8 |
| A | WO 02/30356 A (UNIV MISSISSIPPI) 18 April 2002 (2002-04-18) claims 1-32, 44-47, 53-68; figures ----- | 1-8 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/EP 03/10171

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely:
see FURTHER INFORMATION sheet PCT/ISA/210
2. Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
1-10, 21, 22, 32-34
4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
- No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ EP 03/10171

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-8

process according to present claims 1-8

2. Claims: 9,10, 32,33

compounds (9) according to claims 9 and 10, pharmaceutical compositions and method for treatment

3. Claims: 11, 12

compounds of formula (3) and preparation process

4. Claims: 13,14

compounds of formula (4) and preparation thereof

5. Claims: 15,16

compounds of formula (5) and preparation thereof

6. Claims: 17,18

compounds of formula (6) and preparation process

7. Claims: 19,20

compounds of formula (7) and preparation process

8. Claims: 21,22,34

compounds of formula (8), preparation process and method for treatment using compounds (8)

9. Claims: 23,24

compounds of formula (1) and preparation method

10. Claims: 25,26

compounds of formula XV and preparation process

INTERNATIONAL SEARCH REPORT

International Application No. PCT/ EP 03 /10171

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

11. Claims: 27,28

compounds of formula XVI and preparation process

12. Claims: 29,30

compounds of formula XVII and preparation process

13. Claim : 31

compounds of formula (2)

INTERNATIONAL SEARCH REPORT

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FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 32 and 34 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Claims 21 and 22 mention a substituent R2 referring to "the above given meanings". However, since there are 2 different meanings in the above claims, the characterisation on page 3, lines 1-3 of the description has been taken as a basis for the search.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/03/10171

| Patent document cited in search report | | Publication date | | Patent family member(s) | | Publication date |
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| WO 2004012735 | A | 12-02-2004 | DE WO | 10234975 A1 2004012735 A2 | | 12-02-2004 12-02-2004 |
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